The Future of Clinical Epidemiology

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Clinical Epidemiology

- Numerous opportunities
- Clinical epidemiology calls for collaboration
  - Pharmaco-epidemiology
- Example applications
- Collaboration opportunities

Pharmacoepidemiology

“In practice, Pharmacoepidemiology seeks to frame the benefits of medications against their potential harm in the heterogeneous population of [older] adults who are prescribed the drug. The United States has been slow to create the infrastructure needed to support these studies at a national level. Yet other countries have vigorously begun initiating such infrastructures”

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DoD Statins

- October 1, 1999 interchange of current statins to either simvastatin or cerivastatin
- Majority of subjects to be converted to cerivastatin (60%)

Occurrence of Adverse Events

- Cerivastatin risk for myositis or rhambdomyolysis equal to other statins
- Dual mechanism of elimination via the liver
  - CYP 2C8 major pathway
  - CYP 3A4 minor metabolites
- Micro-dosing
- DoD use – occurrence of adverse events similar to other statins

Baycol Removed From the Market August 2001

- 10 fold greater incidence of fatal rhambdomyolysis
- Occurrence greater at 0.8 mg and among elderly
- Greater interaction with gemfibrozil
  - Alternative pathway

Another Statin Story

Statin Related Muscle Injury

- Clinical question
  - Is statin related adverse events common in the VA
  - How often are statins used concomitantly with interacting therapies (CYP3A4 inhibitors, Gemfibrozil, niacin, Amiodarone,) and does this increase the occurrence of adverse events

The Beginning

- It was originally reported that there were 31 deaths due to Baycol, but that number has increased to 52 deaths, and it is likely to be much higher. The drug's manufacturer, Bayer, confirmed a German government report on august 23 that Baycol was linked to 1,100 cases of muscle weakness.
- It really appears that most of the statin drugs are an accident waiting to happen. Public citizen is seeking black box warning, which is the strongest labeling caution that can be mandated by the FDA. If you are taking Lipitor, Lescol, Zocor, Pravachol, or Mevacor you will want to seriously consider other options immediately.

The Expansion

- **Learn if YOU have a claim against Merck & co., Inc. (Maker of Zocor)**

  Zocor linked to muscle-destroying Rhabdomyolysis

- The Kahn Gauthier law group is investigating possible legal actions against Merck & co., Inc., The manufacturer of the cholesterol-lowering prescription drug Zocor (simvastatin), on behalf of patients prescribed Zocor who have suffered rhabdomyolysis as a side-effect of taking the drug. *Over the past 30 years, our team has been responsible for bringing justice and distributing millions of dollars to thousands of clients from class action and individual settlements.*

Where to Find the Answer

- Data from RCT limited
- Rare event
  1/5000
- Adverse event reporting inadequate

VISN 1 Pharmepi

- Clinical practice
- Large population
- Dynamic cohort
- Misclassification of outcomes of interest
- Rare event 1/5000
- Enough exposure to statin and combination

VISN 1 PharmEpi Database

- 205,472 active users
  - Use of service during any 18-month period
  - Study period Jan 98 – June 2001
- 60,232 received a Statin
  - Majority of use split between Simva and Lova
  - 16,160 also were prescribed to interacting therapies

Occurrences of Elevated CK, Clinical Myositis, and Rhabdomyolysis

- *Elevated CK ≥ 200*
  - 6,899 incidences
  - **10 cases/1000 patient-yr**
- *Clinical myositis*
  - 3,413 cases
  - **5 cases/1000 patient-yr**
- *Combined diagnosis*
  - 114 cases
  - **0.016 cases/1000 pt-yr**

Odds Ratios and 95% CI of Various Outcomes

	Elevated CK	Clinical Myositis	Combined Diagnosis
Any Statin	2.42 (2.29-2.57)	1.59 (1.45-1.74)	2.66 (1.72-4.12)
Statin Combo	4.99 (4.53-5.49)	2.95 (2.51-3.48)	3.92 (1.71-8.98)

Clinical Epidemiology Examples

Antibiotic Resistance Study Objectives

- Determine the rate of treatment failure of select macrolides, quinolones and Augmentin when used as initial therapy for community acquired acute respiratory tract infections (RTIs)
- Determine the cost of treatment RTIs by drug and type of infection

Assumptions

- Antibiotic treatment failure is common (19.6%) with currently available agents
- Treatment failure significantly increases the total cost of treating RTIs (74%)
- Drug resistance under diagnosed as potential cause of treatment failure

Assumptions

- Literature indicate that an antibiotic that would possess a combination of the following characteristics may help reduce treatment failures and costs
  - Short course (5-day) of therapy
  - Effective against resistant organisms
  - Not prone to the emergence of resistance
  - Reasonably priced

Carrier Based/ Land Based Study

- Upper respiratory infections
  - Prevalence
  - Surveillance drug resistance
- Carrier based and land based prophylactic intervention
  - Compare rates of emergence of drug resistance
  - Health services research
    - Return to work – patient reported outcomes
    - Costs
    - Concomitant drug use

The Golden Hour

Improving Outcomes in the Golden Hour

- Predictors of worse outcomes regarding combat related trauma
- Hypothesis
  - Use of NSAIDs chronically may significantly prolong bleeding time
  - Prolonged bleeding time may lead to greater complications
  - Cox-2 inhibitors as preferred pain reliever for forward deployed may avert bleeding complications

Collaboration

- Practicing clinicians
  - MTF
  - Ships and oversees
- Harvard School of Public Health Clinical Effectiveness Program
  - Summer only masters program
  - Clinical epidemiology concentration
  - http://hsph.harvard.edu/clineff/
- MAVERIC

Conclusions